REMARKS

Claims 1, 20-35 and 43-83 were pending and under consideration. In the Office Action mailed May 3, 2002, the PTO requested cancellation of Claims 20-35 and 43-55. Applicants amendment under 37 C.F.R. §1.116 mailed September 3, 2002, was not entered. Applicants hereby submit a Request for Continued Examination and Amendment under 37 C.F.R. §1.114. The PTO has renumbered Claims 43-70 as Claims 56-83 and requested amendment of the Claims to correct dependency. With this Amendment, Applicants amend Claims 1, 56-63, 67-75, 79, 82 and 83 as requested to correct dependency. Applicants hereby cancel claims 20-35 and renumbered claims 43-55, 64-66 and 80-81 without prejudice. Claims 76-78 have been withdrawn from consideration by the PTO as drawn to a non-elected species (ApoA-I agonist-lipid complexes) and are hereby canceled by Applicants without prejudice. New Claims 84-88 have been added. After entry of the instant amendment, Claims 1, 56-63, 67-75, 79, 82-88 are pending. A version with markings to show changes made is attached at Exhibit A. For the Examiner's convenience, a clean copy of all pending claims is attached at Exhibit B.

I. THE AMENDMENT TO THE CLAIMS

For consistency with the PTO's restriction requirement, Claim 1 has been amended to recite, in relevant part, an ApoA-I agonist compound comprising (i) a 15 to 26- residue peptide or peptide analogue according to formula (I) which forms an amphipathic α-helix in the presence of lipids and exhibits at least about 38% LCAT activation activity as compared with human ApoA-I wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X_1 to X_{23} of formula (I). Support for amended Claim 1 can be found in the Claim 1 as originally filed and in the specification, for example, at page 50, line 11 to page 51, line 13.

Claim 1 has also been amended to recite, in relevant part, Z_1 is H_2N-. Support for these amendments to Claim 1 can be found, for example, in Claim 1 as originally filed.

Claims 58-63, 69, 73, 75, 79, 82 and 83 have been amended to correct dependency following re-numbering of the Claims. Claims 1, 56-63, 67-75 and 79 have been amended to recite '15 to 26-residue peptide or peptide analogues' and to remove the term 'deleted'.

Support for amended Claims 1, 56-63, 67-75 and 79 may be found in the claims as originally filed and in the specification, for example, at page 50, lines 11 to page 51, line 13.

Claims 82 and 83 have been amended to recite pharmaceutical compositions of ApoA-I agonists which are a lyophilized powder and a solution and to remove non-elected subject matter (ApoA-I agonist-lipid complexes). Support for amended Claims 82 and 83 can be found, for example, in page 85, line 5 to page 87, line 25.

The claims have been amended to generally recite a 15 to 26- residue peptide or peptide analogue wherein one or two helical turns is deleted from formula I. The helical turns that are deleted are comprised of residues X_1 through X_{23}. The deletion of one or two helical turns can be via the removal of 3 or 4 consecutive residues or more than one group of 3 or 4 consecutive residues (providing for the deletion of 6, 7 or 8 residues).

As the amendments to the Claims are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry thereof is therefore respectfully requested.

II. THE NEW CLAIMS

New Claim 84 recites the N-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1. New Claim 85 recites, in relevant part, that the N-terminally blocking group is selected from the group consisting of acetyl, formyl and dansyl. New Claim 86 recites the C-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1. New Claim 87 recites, in relevant part, that the C-terminally blocking group is methyl. New Claim 88 recites the N-terminally and C-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1.

Support for new Claims 84-88 can be found in the specification, for example, at page 52, line 11 to page 53, line 8. As the new Claims are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry thereof is therefore respectfully requested.

III. RESTRICTION

In the Office Action mailed May 3, 2002, the PTO issued a further restriction in the pending matter. The PTO asserted that a restriction is necessary between ApoA-I peptide agonists and peptide-lipid complexes. Given that Applicants had received an action on the

merits for ApoA-I agonists, the PTO asserted that ApoA-I agonists had been constructively elected. Accordingly, Claims 76 and 78 have been withdrawn from consideration by the PTO. Applicants hereby formally cancel Claims 76 and 78 without prejudice.

Applicants reserve the right to pursue any unclaimed subject matter in one or more continuation, divisional or continuation-in-part applications.

IV. CLAIM REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 56-75, 79-83 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being unclear as to the meaning of 'a deleted peptide or peptide analogue'. Claims 64-66, 80 and 81 have been canceled rendering rejection of these claims moot.

Applicants submit that Claims 1, 56-63, 67-73, 75 and 79 are clear. However, merely to expedite passage of the claims to allowance, Claims 1, 56-63, 67-75 and 79 have been amended to recite ApoA-I agonists that are 15 to 26-residue peptides or peptide analogues. Applicants submit that amended Claims 1, 56-63, 67-75 and 79 are clear and respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

V. CLAIM OBJECTIONS

Claims 1, 65, 67-75, 79-83 stand objected to for allegedly reading on non-elected subject matter (full-length ApoA-I agonists). Claims 64-65, 80 and 81 have been canceled without prejudice rending the rejection of these claims moot.

Amended Claim 1 recites, in relevant part, an ApoA-I agonist compound comprising (i) a 15 to 26- residue peptide or peptide analogue according to formula (I) which forms an amphipathic α-helix in the presence of lipids and exhibits at least about 38% LCAT activation activity as compared with human ApoA-I wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X_1 to X_{23} of formula (I). Applicants respectfully submit that Claims 1, 67-75, 79 and 82-83 do not read on non-elected subject matter and respectfully request that the objection be withdrawn.

VI. CLAIM REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1, 57 and 60-63 stand rejected as allegedly containing new matter as to 'two' helical turns. Claim 64 stands rejected as allegedly containing new matter in that Claim 64

recites 'residue 18 should not be deleted.' Claims 1, 56-75, 79-83 stand rejected for allegedly not being enabled.

A. NEW MATTER

To satisfy the written description requirement, the specification must convey with reasonable clarity to those skilled in the art that he or she was in possession of the claimed subject matter. *See, Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985), *In re Wilder* 222 USPQ 369, 372 (Fed. Cir. 1984). The specification need not provide written description support in exactly the same words as are used in the claims. *Application of Luckach* 169 USPQ 795, 796 (CCPA 1971).

i. Two helical turns

The Patent Office rejects Claims 1, 57 and 60-63 as allegedly containing new matter, in that they recite deletion of two helical turns.

Applicants submit that the specification as originally filed fully supports the term 'two' helical turns. Applicants refer the Patent Office to the specification at page 50, lines 11 to 19. Therein is described peptides with 18 or even 15 residues. The specification describes ApoA-I agonists according to formula (I) that are, for example, 22 to 29 residues. (Page 51, lines 23 to 32). The specification also describes at page 51, lines 1 to 13 that an idealized α-helix contains 3.6 residues per turn, equivalent to 3 or 4 residues. The specification also describes that ApoA-I agonists may contain as few as 15 residues. It is apparent to one of skill in the art that deletion of six, seven or eight residues, for example, from a 29 residue ApoA-I agonist peptide would be the equivalent of deleting two helical turns.

The specification teaches that the ApoA-I agonists are amphipathic α-helices that bind to lipids. (See Section VI, B, below). Deletion of residues from the ApoA-I agonists while maintaining α-helical structure is taught in the specification. The deletion of residues can be such that one or two helical turns are deleted. Thus, one of skill in the art would recognize that Applicants had possession of ApoA-I agonists with one or two helical turns deleted.

Applicants therefore respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

ii. Deletion of X_{18}

The Patent Office rejects Claim 64 as allegedly containing new matter, in that it recites the deletion of residue 18. Claim 64 has been canceled rendering rejection of the claim moot. Applicants therefore respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

B. ENABLEMENT

Claims 1, 56-75 and 79-83 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not being enabled as to deleted peptides and deleted peptide analogues. Claims 64-67, 80 and 81 have been canceled rendering rejection of these claims moot. Applicants respectfully traverse the rejection of the remaining claims. Applicants submit that the breadth of these Claims is commensurate in scope with the abundant teachings of the specification and fully enable one of skill in the art to make and use the 15 to 26- residue ApoA-I agonist peptides without undue experimentation.

A claim is enabled if one of skill in the art, guided by Applicant's disclosure, can make and use the claimed invention without undue experimentation. *See, Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Wands*, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is not undue. *See, In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976).

Among the factors to be considered when determining whether the necessary experimentation is undue are the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See, In re Wands*, 8 U.S.P.Q.2d at 1404. In rejecting a claim for lack of enablement, the Examiner should cite any of these factors that are relevant, and specific technical reasons are always required. *See,* M.P.E.P. at §§ 2164.01(a) 2164.04; *In re Wands*, 8 U.S.P.Q.2d at 1404.

All questions of enablement are evaluated against the claimed subject matter. *See,* MPEP §2164.08. As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art

by the disclosure is commensurate with the scope of protection sought by the claims (*Id.* citing *In re Moore*, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971).

The PTO alleges that the claims are broadly drawn to deletion analogues wherein one or two helical turns are optionally deleted resulting in a 15 to 26-residue deleted peptide or peptide analogue, resulting in a large number of deletion analogues lacking any defined peptide core structure.

Amended independent Claim 1 recites, in relevant part, an ApoA-I agonist compound comprising (i) a 15 to 26- residue peptide or peptide analogue according to formula (I) which forms an amphipathic α-helix in the presence of lipids and exhibits at least about 38% LCAT activation activity as compared with human ApoA-I wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X_1 to X_{23} of formula (I). Claim 1 has been amended to more clearly recite structural features and activity of the 15 to 26-residue ApoA-I agonist peptides and peptide analogues.

The Patent Office asserts that the specification does not disclose a *core structure* required for the deleted peptides to maintain their biological activity. (Office Action mailed May 3, 2002, paper 12, page 6, emphasis added). In addition, the Patent Office asserts that there is insufficient guidance and working examples in regard to deletion analogs such that one skilled in the art allegedly could not make or use the invention with the claimed breadth without an undue amount of experimentation. (*Id.* at 7.)

The ApoA-I agonists form amphipathic α-helices in the presence of lipids, bind to lipids, form pre β-like or HDL like complexes, activate LCAT, increase serum HDL concentration and promote cholesterol efflux. (Page 17, lines 18 to 27). The ApoA-I agonists' activity is due to their ability to form amphipathic α-helices in the presence of lipids. Peptides that exhibit greater than about 60% helicity exhibit a high degree of biological activity, as measured by LCAT activation. (*See, e.g.* page 63, line 21 to line 37 and Table IV). An amphipathic α-helix is a secondary structure comprising individual amino acids that form a helix having a hydrophobic face and a hydrophilic face. As taught by the specification, any one amino acid can be substituted with another amino acid of a similar hydrophibicity while maintaining the overall amphipathic α-helix. (*See, e.g.* page 28, line 28 to page 30, line 15). Thus, the function of the ApoA-I agonists does not require the presence

of a particular residue or a particular 'core structure', but rather the ability to form a secondary structure, namely an amphipathic α-helix in the presence of lipids.

Dependent Claims 68-75 recite 15 to 26-residue ApoA-I agonist peptides with defined parameters such as mean hydrophobicity, mean hydrophobic moment, mean hydrophobicity of the hydrophobic face, and the pho angles. (Page 30, line 24 to page 32, line 23). For example, the ApoA-I agonists have a mean hydrophobic moment, $< \mu_H >$, from about 0.45 to about 0.65 and preferably from about 0.50 to about 0.60. The mean hydrophobicity, $<H_o>$, is from about -0.050 to about -0.070 and preferably from about -0.030 to about -0.055. The ApoA-I agonists have a mean hydrophobicity of the hydrophobic face, $< H_o^{pho} >$, from about 0.90 to about 1.20 and preferably from about 0.94 to about 1.10. The pho angle is from about 160° to about 220° and preferably from about 180° to about 200°.

Dependent Claims 58-63 recite 15 to 26-residue ApoA-I agonist peptides formed by the deletion of 3 or 4 consecutive residues (comprising one helical turn) or a contiguous or non-contiguous set of 3 or 4 consecutive residues (comprising two helical turns).

The specification teaches that an α-helix contains 3.6 residues per turn and that in preferred embodiments, groups of 3-4 consecutive or non-consecutive amino acids are deleted. (Page 51, lines 1 to 13). The characteristics of the α-helical hydrogen bonds are well known in the art and cited throughout the specification. For example, the specification provides that an α-helix is stabilized by hydrogen bond formation at positions *i* to *i*+3 of the helix. (Page 36, lines 3 to 7). References in the art describing the nature of an α-helix are provided in the specification and incorporated by reference, for example, Chao and Fasman (page 43, line 14), Schiffer and Edmundson (page 29, lines 2 to 3), Marqusee (page 36, lines 6 to 7), Lim (page 29, lines 17 to 18) and Eisenberg (page 29, lines 22 to 23; page 30, lines 31 to 32; page 31, line 8 and lines 21 to 22).

It is well established that secondary structure is determined not by individual residues but by the number of residues adjacent that share physical features. Schiffer and Edmundson in 1967 (*Biophysical Journal* 7: 121-135) demonstrated that in a two-dimensional projection of a helical wheel the hydrophobic residues tend to be clustered in the n ± 3, n, n ± 4 positions of adjacent helical turns. Chou and Fasman in 1978 (*Ann. Rev. Biochem.* 47: 251-76) developed an accurate method of predicting α-helices and β-sheets in proteins based the clustering of residues with similar physical and chemical characteristics. In the Chou-Fasman methodology, certain secondary structural features are predicted when a critical mass of like

residues are present in clusters. For example, a cluster of four out of six helix forming residues will nucleate a helix. A cluster of three β-sheet residues out of five will nucleate a β-sheet. Schiffer and Edmundson and Chou and Fasman are references well-known to those of skill in the art and incorporated by reference in the specification. The specification teaches that the amphipathic α-helices formed by the 15 to 26-residue ApoA-I agonist peptides have hydrophilic and hydrophobic faces. (For example, page 22, lines 5 to 17; Figs. 2A and 2B and page 29, lines 16 to 29). Having opposing hydrophilic and hydrophobic faces oriented along the axis of the helix provides amphipathicity to the α-helix. These hydrophilic and hydrophobic faces are created by the juxtaposition of hydrophobic and hydrophilic amino acid residues in the peptide, as is known to one of skill in the art. The characterization of amino acid residues as hydrophobic or hydrophilic is known in the art and provided in the specification, for example, at page 41, line 1 to page 42, line 19. Consequently, selecting a cluster of like residues comprising one or two helical turns would be well within the capabilities of one of skill in the art.

The specification clearly teaches one of skill in the art how to make and use 15 to 26-residue ApoA-I agonists that form amphipathic α-helices in the presence of lipids without undue experimentation. Figures 1-5 provide Schiffer-Edmundson wheels of the amphipathic helices demonstrating the periodic arrangement of hydrophobic and hydrophilic residues. One face of the helix is occupied by hydrophobic residues and the other face occupied by hydrophilic residues, as explained in the specification, for example, at page 28, line 28 to page 30, line 15. Applicants submit that one of skill in the art, guided by the specification, can delete at least one and up to eight residues and maintain the amphipathic α-helical structure illustrated in the Schiffer-Edmundson diagram.

The α-helical structure of the 15 to 26-residue ApoA-I agonist peptides can be determined by calculating certain parameters, as is taught in the specification. Methods of calculating these parameters and preferred values of these parameters are taught in abundance in the specification and capable of being performed by one of skill in the art without undue experimentation. *See,* the specification at page 30, line 24 to page 33, line 2 and references cited therein, including, Eisenberg, 1984 *Ann. Rev. Biochem.* 53: 595-623 and Eisenberg, 1984 *J. Mol. Biol.* 179: 125-142. Thus, given the extensive teaching of the specification, one of skill in the art can use the mean hydrophobic moment, $< \mu_H >$, the mean hydrophobicity, $<H_o>$, the mean hydrophobicity of the hydrophobic face, $< H_o^{pho} >$, and the pho angle to make

deleted ApoA-I agonists while maintaining the α-helical structure and ApoA-I agonist activity. In addition, the breadth of the Claims, specifically Claims 68-75 are commensurate with the scope of enablement provided to one of skill in the art.

Biological activity of the 15 to 26-residue ApoA-I agonist peptides is recited in Claim 1 as being at least about 38% as compared to human ApoA-I. Again, the specification teaches and describes how LCAT activation activity can be determined without undue experimentation. Example 8 teaches an LCAT activation assay that can be practiced by one of skill in the art. (Page 102, line 18 to page 122, line 7). The scope of the teaching of Example 8 is clearly commensurate with the breadth of the Claims, particularly independent Claim 1.

Furthermore, lipid binding activity of the ApoA-I agonists can be verified experimentally in a manner that does not require undue experimentation. Indeed, such experimentation is routine to one of ordinary skill in the art. For example, when ApoA-I agonists are added to a turbid solution of lipids in water and mixed, the solution clarifies as the ApoA-I agonists bind to the lipids. Such an experiment is clearly within ordinary skill. The formation of amphipathic α-helices can also be determined, without undue experimentation, using the method of co-lyophilization. (Page 129, line 1 to page 130, line 32). Peptide/lipid binding can be verified by mixing the peptides and lipids in miscible solvents, the peptides forming amphipathic α-helices in the presence of lipids. The peptide/lipid mixture is lyophilized and the lyophilized powder then reconstituted. Chromatographic spectra of the reconstituted mixture exhibits a single peak at 254 nm. Thus, one of skill in the art can use a simple and quick lipid binding experiment, without undue experimentation, to make the 15 to 26- residue ApoA-I agonist peptides.

Moreover, the specification provides abundant teachings of methods and techniques known to those of skill in the art for verifying α-helical structure, including CD spectroscopy, fluorescence and NMR spectroscopy. (page 94, line 1 to page 96, line 20; page 96, line 23 to page 99, line 17 and page 99, line 20 to page 102, line 15). For example, the helicity of the 15 to 26- residue ApoA-I agonist peptides can be determined quickly and simply by CD spectroscopy by one of skill in the art. The conditions under which ApoA-I agonist helicity is determined are described on page 94, line 8 to page 96, line 20. The exemplary peptide (SEQ ID NO: 146) contains significant helicity (86% helicity) at a concentration of 5 μM. (Page 95, lines 29 to 31). Those peptides that exhibited ≥38% LCAT activation exhibited ≥ 60% helical structure in the case of unblocked peptides containing 22 or more residues or

blocked peptides containing 18 or fewer residues; ≥ 40% helicity in the case of unblocked peptides containing 18 or fewer amino acids. (Page 96, lines 3 to 20 and Table X). Use of CD spectroscopy is routine to one of skill in the art and the degree of experimentation needed to verify helicity of the ApoA-I agonists is not undue. *See,* specification at page 95, and references cited therein *e.g.*, Chen *et al.*, 1974, *Biochemistry* 13: 3350-3359, Provencher and Glockner, 1981, *Biochemistry* 20: 33-37 and Venyaminov *et al.*, 1993, *Anal. Biochem.* 214: 17-24. Thus, one of skill in the art could use peptide helicity as determined by CD spectroscopy to make deleted ApoA-I agonists.

Claims 1, 56-63, 67-75, 79, 82 and 83 are fully enabled. The breadth of Claims 1, 56-63, 67-75, 79, 82 and 83 are commensurate with the scope of enablement provided to one of skill in the art by the numerous examples provided. The specification describes physical and structural properties of ApoA-I agonists important for activity. The specification describes the use of standard tools and techniques, such as Schiffer-Edmondson wheel and CD spectroscopy, which can be used without undue experimentation to make and use ApoA-I agonists of various lengths, including 15 to 26- residue peptides and peptide analogues. Therefore, one of skill in the art, guided by the specification can make and use 15 to 26-residue ApoA-I agonists without undue experimentation. Applicants therefore respectfully request that the rejection be withdrawn.

VII. DOUBLE PATENTING

The Patent Office asserts that the Terminal Disclaimer over U.S. Patent Nos. 6,004,925, 6,037,323 and 6,265,377 is defective, allegedly because it lists six inventors. Applicants submit herewith a Terminal Disclaimer properly identifying the six individuals as owners of the present invention.

Claims 1, 57-76 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over copending Application No. 09/453,841. Applicants hereby request that the rejection be held in abeyance until an indication of patentable subject matter is given, at which point a Terminal Disclaimer may be filed.

CONCLUSION

Applicants submit that Claims 1, 56-63, 67-75, 79, 82-88 satisfy all the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly solicited.

No fee in addition to the fee for a Request for Continued Examination is believed due with this Amendment. However, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP, U.S. Deposit Account No. 16-1150 (Order No. 9196-018-999). A copy of this sheet is enclosed for accounting purposes.

Respectfully submitted,

Date December 18, 2002

42,983

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EXHIBIT A

Claim Amendments: Version with Markings to Show Changes Made

1. (Amended) An ApoA-I agonist compound comprising:

(i) a 15 to [29] 26-residue peptide or peptide analogue according to formula (I) which forms an amphipathic α-helix in the presence of lipids [and which comprises formula (I)] and exhibits at least about 38% LCAT activation activity as compared with human ApoA-I wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X_1 to X_{23} of formula (I):

$$Z_1\text{-}X_1\text{-}X_2\text{-}X_3\text{-}X_4\text{-}X_5\text{-}X_6\text{-}X_7\text{-}X_8\text{-}X_9\text{-}X_{10}\text{-}X_{11}\text{-}X_{12}\text{-}X_{13}\text{-}X_{14}\text{-}X_{15}\text{-}X_{16}\text{-}X_{17}\text{-}X_{18}\text{-}X_{19}\text{-}X_{20}\text{-}X_{21}\text{-}X_{22}\text{-}X_{23}\text{-}Z_2$$

or a pharmaceutically acceptable salt thereof, wherein:

X_1 is Pro (P), Ala (A), Gly (G), Gln (Q), Asn (N), Asp (D) or D-Pro (p);

X_2 is an aliphatic residue;

X_3 is a Leu (L) or Phe (F);

X_4 is Glu (E)

X_5 is an aliphatic residue;

X_6 is Leu (L) or Phe (F);

X_7 is Glu (E) or Leu (L);

X_8 is Asn (N) or Gln (Q);

X_9 is Leu (L);

X_{10} is Leu (L), Trp (W) or Gly (G);

X_{11} is an acidic residue;

X_{12} is Arg (R);

X_{13} is Leu (L) or Gly (G);

X_{14} is Leu (L), Phe (F) or Gly (G);

X_{15} is Asp (D);

X_{16} is Ala (A);

X_{17} is Leu (L);

X_{18} is Asn (N) or Gln (Q);

X_{19} is a basic residue;

X_{20} is a basic residue;

X_{21} is Leu (L);

X_{22} is a basic residue;

X_{23} is absent or a basic residue;

Z_1 is $\underline{H_2N-}$ [R_2N- or RC(O)NR-];

Z_2 is -C (O) NRR or -C (O) OR;

each R is independently -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl, 5-20 membered heteroaryl or 6-26 membered alkheteroaryl or a 1 to 7-residue peptide or peptide analogue in which one more bonds between residues 1-7 are independently a substituted amide, an isostere of an amide or an amide mimetic;

each "-" between residues X_1 to X_{23} and between residues of the peptide to Z_2 independently designates an amide linkage, a substituted amide linkage, an isostere of an amide or an amide mimetic; or

[(ii) a 15 to 26-residue deleted peptide or peptide analogue according to formula (I) in which one or two helical turns of the peptide or peptide analogue are optionally deleted]

an N- terminally blocked form, a C-terminally blocked form, or an N- and C-terminally blocked form of formula (I).

56. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which one helical turn is deleted.

57. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which three, four, six, seven or eight residues X_1, X_2, X_3, X_4, X_5, X_6, X_7, X_8, X_9, X_{10}, X_{11}, X_{12}, X_{13}, X_{14}, X_{15}, X_{16}, X_{17}, X_{18}, X_{19}, X_{20}, X_{21} and X_{22} are deleted.

58. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which 3 consecutive residues are deleted.

59. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which 4 consecutive residues are deleted.

60. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which two non-contiguous sets of 3 consecutive residues are deleted.

61. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which two non-contiguous sets of 4 consecutive residues are deleted.

62. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which one set of 3 consecutive residues and one set of 4 consecutive residues are deleted.

63. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [44] 57, in which 6, 7 or 8 consecutive residues are deleted.

67. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1 in which:
the "-" between residues designates -C (O) NH- ;
Z_1 is H_2N- ; and
Z_2 is -C (O) OH or a salt thereof.

68. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which the mean hydrophobic moment, $<\mu_H>$, is [about] 0.45 to [about] 0.65.

69. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [55] 68, in which the mean hydrophobic moment, $<\mu_H>$, is [about] 0.50 to [about] 0.60.

70. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which the mean hydrophobicity, $<H_o>$, is [about] -0.050 to [about] -0.070.

71. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which the mean hydrophobicity, $<H_o>$, is [about] -0.030 to [about] -0.055.

72. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which the mean hydrophobicity of the hydrophobic face, $<H_o^{pho}>$, is [about] 0.90 to [about] 1.20.

73. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [59] 72, in which the mean hydrophobicity of the hydrophobic face, $<H_o^{pho}>$, is [about] 0.94 to [about] 1.10.

74. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim 1, in which the pho angle is [about] 160° to [about] 220°.

75. (Amended) The 15 to 26-residue [deleted] peptide or peptide analogue of Claim [61] 74, in which the pho angle is 180° to [about] 200°.

79. (Amended) A pharmaceutical composition comprising an ApoA-I agonist compound and a pharmaceutically acceptable carrier, excipient or diluent, wherein the ApoA-I agonist compound is a 15 to 26- residue [deleted] peptide or peptide analogue according to Claim 1 or [44] 57.

82. (Amended) The pharmaceutical composition of Claim [80 or 81] 79 [in] which [the ApoA-I agonist compound-lipid complex] is [in the form of] a lyophilized powder.

83. (Amended) The pharmaceutical composition of Claim [80 or 81] 79 [in] which [the ApoA-I agonist compound-lipid complex] is [in the form of] a solution.

Exhibit B

Claim Amendments: Pending Claims After Entry of the Instant Amendment

1. (Amended) An ApoA-I agonist compound comprising:

(i) a 15 to 26- residue peptide or peptide analogue according to formula (I) which forms an amphipathic α-helix in the presence of lipids and exhibits at least about 38% LCAT activation activity as compared with human ApoA-I wherein one or two helical turns are deleted from formula (I), wherein a helical turn consists of 3 to 4 consecutive residues selected from residues X_1 to X_{23} of formula (I):

$$Z_1\text{-}X_1\text{-}X_2\text{-}X_3\text{-}X_4\text{-}X_5\text{-}X_6\text{-}X_7\text{-}X_8\text{-}X_9\text{-}X_{10}\text{-}X_{11}\text{-}X_{12}\text{-}X_{13}\text{-}X_{14}\text{-}X_{15}\text{-}X_{16}\text{-}X_{17}\text{-}X_{18}\text{-}X_{19}\text{-}X_{20}\text{-}X_{21}\text{-}X_{22}\text{-}X_{23}\text{-}Z_2$$

or a pharmaceutically acceptable salt thereof, wherein:

X_1 is Pro (P), Ala (A), Gly (G), Gln (Q), Asn (N), Asp (D) or D-Pro (p);

X_2 is an aliphatic residue;

X_3 is a Leu (L) or Phe (F);

X_4 is Glu (E)

X_5 is an aliphatic residue;

X_6 is Leu (L) or Phe (F);

X_7 is Glu (E) or Leu (L);

X_8 is Asn (N) or Gln (Q);

X_9 is Leu (L);

X_{10} is Leu (L), Trp (W) or Gly (G);

X_{11} is an acidic residue;

X_{12} is Arg (R);

X_{13} is Leu (L) or Gly (G);

X_{14} is Leu (L), Phe (F) or Gly (G);

X_{15} is Asp (D);

X_{16} is Ala (A);

X_{17} is Leu (L);

X_{18} is Asn (N) or Gln (Q);

X_{19} is a basic residue;

X_{20} is a basic residue;

X_{21} is Leu (L);

X_{22} is a basic residue;

X_{23} is absent or a basic residue;

Z_1 is H_2N- ;

Z_2 is -C (O) NRR or -C (O) OR;

each R is independently -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl, 5-20 membered heteroaryl or 6-26 membered alkheteroaryl or a 1 to 7-residue peptide or peptide analogue in which one more bonds between residues 1-7 are independently a substituted amide, an isostere of an amide or an amide mimetic; and

each "-" between residues X_1 to X_{23} and between residues of the peptide to Z_2 independently designates an amide linkage, a substituted amide linkage, an isostere of an amide or an amide mimetic; or

an N- terminally blocked form, a C-terminally blocked form, or an N- and C-terminally blocked form of formula (I).

56. (Amended) The 15 to 26-residue peptide or deleted peptide analogue of Claim 1, in which one helical turn is deleted.

57. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which three, four, six, seven or eight residues X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , X_7 , X_8 , X_9 , X_{10} , X_{11} , X_{12} , X_{13} , X_{14} , X_{15} , X_{16} , X_{17} , X_{18} , X_{19} , X_{20} , X_{21} and X_{22} are deleted.

58. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which 3 consecutive residues are deleted.

59. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which 4 consecutive residues are deleted.

60. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which two non-contiguous sets of 3 consecutive residues are deleted.

61. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which two non-contiguous sets of 4 consecutive residues are deleted.

62. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which one set of 3 consecutive residues and one set of 4 consecutive residues are deleted.

63. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 57, in which 6, 7 or 8 consecutive residues are deleted.

67. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1 in which:
the "-" between residues designates -C (O) NH- ;
Z_1 is H_2N- ; and
Z_2 is -C (O) OH or a salt thereof.

68. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which the mean hydrophobic moment, $<\mu_H>$, is 0.45 to 0.65.

69. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 68, in which the mean hydrophobic moment, $<\mu_H>$, is 0.50 to 0.60.

70. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which the mean hydrophobicity, $<H_o>$, is -0.050 to -0.070.

71. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which the mean hydrophobicity, $<H_o>$, is -0.030 to -0.055.

72. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which the mean hydrophobicity of the hydrophobic face, $<H_o^{pho}>$, is 0.90 to 1.20.

73. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 72, in which the mean hydrophobicity of the hydrophobic face, $<H_o^{pho}>$, is 0.94 to 1.10.

74. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 1, in which the pho angle is 160° to 220°.

75. (Amended) The 15 to 26-residue peptide or peptide analogue of Claim 74, in which the pho angle is 180° to 200°.

79. (Amended) A pharmaceutical composition comprising an ApoA-I agonist compound and a pharmaceutically acceptable carrier, excipient or diluent, wherein the ApoA-I agonist compound is a 15 to 26-residue peptide or peptide analogue according to Claim 1 or 57.

82. (Amended) The pharmaceutical composition of Claim 79 which is a lyophilized powder.

83. (Amended) The pharmaceutical composition of Claim 79 which is a solution.

84. (New) The N-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1.

85. (New) The 15 to 26-residue peptide or peptide analogue of Claim 84 in which the N-terminally blocking group is selected from the group consisting of acetyl, formyl and dansyl.

86. (New) The C-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1.

87. (New) The 15 to 26-residue peptide or peptide analogue of Claim 86 in which the C-terminally blocking group is methyl.

88. (New) The N-terminally and C-terminally blocked form of the 15 to 26-residue peptide or peptide analogue of Claim 1.